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The Changes in Axial and Radial Diffusivity in a Patient with Clinically Mild Encephalitis/Encephalopathy with a Reversible Splenial Lesion

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Case Report

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Multiple studies have established that mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) exhibits reversible diffusion restriction in the white matter, including the splenium. There have been a few previous reports of the change in fractional anisotropy (FA) of MERS cases. Herein, we report the longitudinal changes in axial and radial diffusivity (AD and RD), and FA in a 15-year-old boy patient with MERS. Our case demonstrated that a MERS lesion had a significant drop of AD in the early period and gradual recovery. On the contrary, RD did not show any significant change.

Keywords: Diffusion tensor imaging; Axial diffusivity; Radial diffusivity; Fractional anisotrophy; MERS

INTRODUCTION

It is well known that clinically mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) exhibits reversible diffusion restriction in the white matter, including the splenium. However, previous reports have mostly described DWI findings. Diffusion parameter evaluation using diffusion tensor imaging (DTI) has recently been reported, and the reports described the change in fractional anisotropy (FA) of the MERS cases (1-4). We report the longitudinal changes in axial and radial diffusivity (AD and RD), and FA in a MERS patient.

CASE REPORT

A 15-year-old boy visited our outpatient clinic with a headache and dizziness a day before admission. Three days before admission, he had abdominal pain and diarrhea, and the symptoms worsened. Headache with chills developed two days before admission. Dizziness and balance discomfort also occurred. MRI was done on the day of admission. The routine MR imaging and DTI were obtained (Ingenia 3.0T CX, Philips Medical Systems, Best, the Netherlands). DTI sequence was acquired with the following protocol: repetition time/echo time, 5915/74 ms; six diffusion-encoding directions, b

= 1000 s/mm^2; voxels of 1.7 × 1.7 × 3 mm^3). DTI showed a well-circumscribed ovoid lesion within the splenium of the corpus callosum that had restricted diffusion on DTI. We analyzed the DTI data using diffusion analysis software (IntelliSpace Portal 8.0, Philips Medical Systems, Best). Quantitative values of FA, AD, RD, and apparent diffusion coefficient (ADC) were measured by manually placing regions of interest (ROIs). The initial diffusion parameter of the splenial lesion were: 0.54 × 10^{-3} mm^2/sec; RD = 0.18 × 10^{-3} mm^2/sec; ADC = 0.3 × 10^{-3} mm^2/sec; and FA = 0.63 (Figs. 1, 2). Electroencephalography demonstrated a normal basic rhythm and sleep background activity without paroxysmal discharges. There was no significant pleocytosis in the CSF test done on the second day of admission, and there were no viral findings in Influenza A, B, or other viral studies. Neurological examination showed no definite focal neurologic sign. The splenial lesion gradually improved in the follow-up DTI imaging done at 1-week intervals, and the abnormality of the diffusion parameters showed restoration as follows: 1) second DTI - AD = 1.16 × 10^{-3} mm^2/sec; RD = 0.23 × 10^{-3} mm^2/sec; ADC = 0.54 × 10^{-3} mm^2/sec; FA = 0.77; 2) third DTI - AD = 1.67 × 10^{-3} mm^2/sec; RD = 0.19 × 10^{-3} mm^2/sec; ADC = 0.68 × 10^{-3} mm^2/sec; and FA = 0.86 in the third DTI (Figs. 1, 2). The longitudinal changes of the DTI parameters are summarized in Table 1. The patient's headache and dizziness resolved completely.

DISCUSSION

In our case, we discovered short-term longitudinal changes in FA, AD, and RD of the MERS. Our case showed that reversible diffusion restriction of the MERS lesion occurred mainly in AD, and the change of water diffusion was not significant in RD. The changes in AD may have
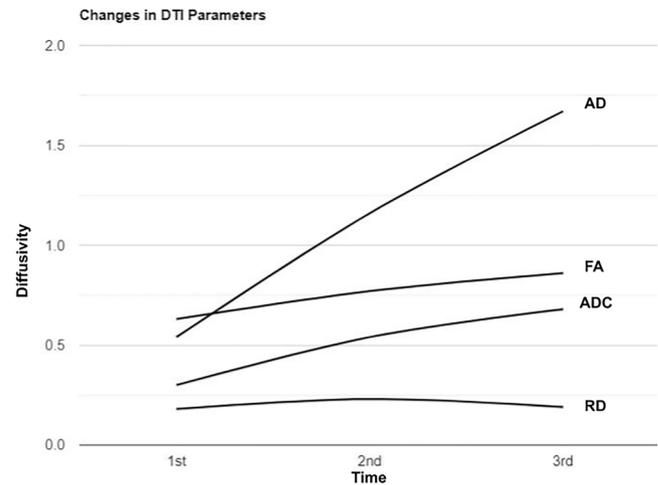

Fig. 2. Serial change in the diffusivity of the MERS. Initially, AD decreased markedly; ADC and FA decreased slightly. In the follow-up DTI, AD increased steeply; FA, and ADC increased gradually. RD showed little change.
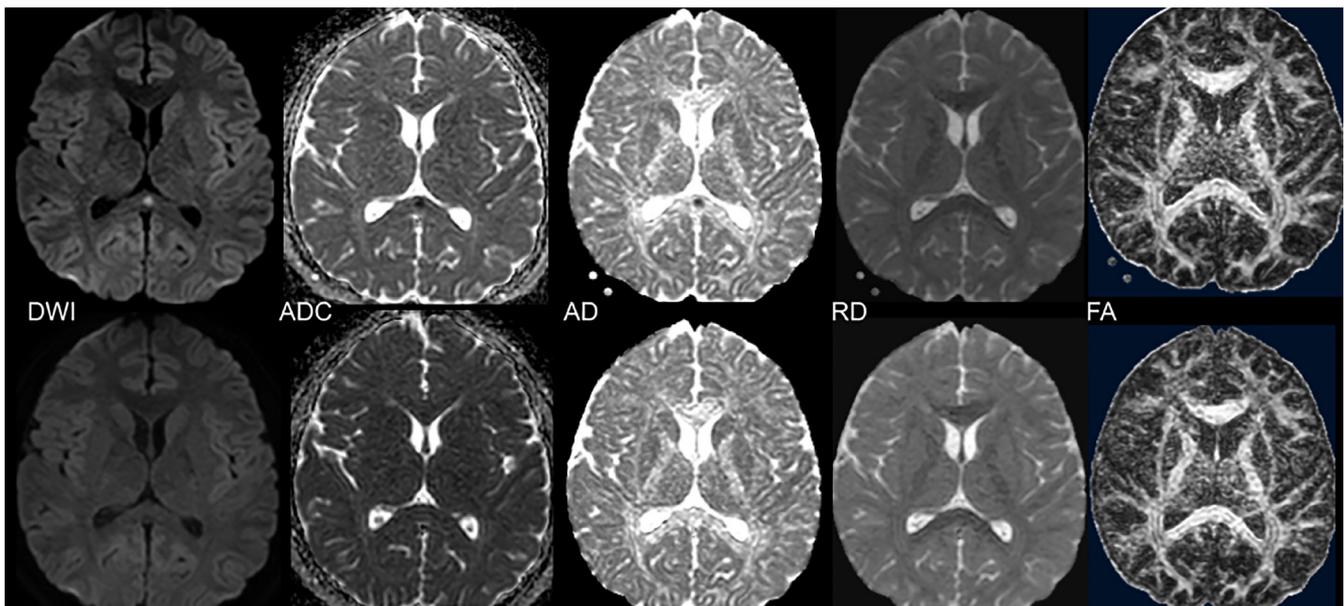

Fig. 1. Upper row: In the DTI image at the time of admission, the splenial lesion has a definite high signal on the DWI, and the reduction of ADC and AD is visible at first glance. The decrease in RD is not apparent, and the change in FA is less noticeable. Bottom row: Follow-up DTI image revealed resolution of diffusion abnormality.

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been caused by changes in axoplasmic flow or axonal diameters (5-7). Toxic or ischemic injury can also cause a decrease in AD (6). Reduced axoplasmic flow or transient decrease in the axonal diameter can lead to a decrease in AD (5-7). In MERS, the reversible diffusion reduction of the water molecules has been described as being caused by intramyelin edema or acute inflammatory cell infiltration (8). Intramyelin edema may reduce axonal diameter transiently due to edema within the myelin layer. In addition, acute neuroinflammation with inflammatory cell infiltration has been reported to reduce axoplasmic flow (9, 10). Although we cannot pinpoint the exact pathophysiological mechanism, our case shows that a lesion in MERS can lead to a reversible decrease in AD. In our case, RD showed little change from the beginning to the follow-up. Such little change suggests that MERS, in our case, had little damage to the axonal membrane or myelin layer.

Looking at five MERS cases that reported FA change, there were three cases in which recovery after initial FA reduction occurred as in our case (1, 2, 4), and in two cases, there was little change in FA (2, 3). The change of DTI parameters in the five cases are summarized in Table 2. The changes in the three eigenvalues of the diffusion tensor

(λ1, λ2, λ3) can influence FA. If the three eigenvalues are all together reduced at an appropriate rate, there may be little change in FA, as in the case of hyperacute cerebral infarction (11, 12). In the previous two cases with little change in FA, we speculate that the three eigenvalues are likely to have shown such a decline.

We obtained DTI using six diffusion gradient directions (DGD). According to the previous studies, the use of more DGD than 21 directions can increase diffusion parameter measurement accuracy and reduce error bias if signal averaging is enough. Also, when using six DGD for DTI, FA, λ1, and λ2 are a bit higher, and λ3 is slightly lower than that of DTI with higher DGDs (13-15). Since we acquired DTI with the same protocol, the diffusion parameter variability due to the protocol change might be minimal. However, it was a limitation that DTI was not optimal for the diffusion parameter evaluation in our case. Since this is only a single case, and the causes of MERS are diverse, one cannot generalize the diffusivity change in the MERS as a significant decrease in AD and subsequent recovery seen in our case. More studies that track changes in AD and RD of the MERS cases are needed.

Conflicts of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethics Approval

This study was done in accordance with the Declaration of Helsinki (1964) and its later amendments. This study was approved by the Institutional Review Board.

Table 1. Serial Changes in the DTI Parameters

	ADC	AD	RD	FA
1st day	0.3 ± 0.07	0.54 ± 0.13	0.18 ± 0.06	0.63 ± 0.13
8th day	0.54 ± 0.07	1.16 ± 0.19	0.23 ± 0.06	0.77 ± 0.09
15th day	0.68 ± 0.14	1.67 ± 0.11	0.19 ± 0.07	0.86 ± 0.09
Normal range	1.06 ± 0.15*	1.74 ± 0.15**	0.35 ± 0.16**	0.61 ± 0.06*

Normal range * from reference (16)
Normal range ** from reference (17)
AD = axial diffusivity; ADC = apparent diffusion coefficient; FA = fractional anisotropy; RD = radial diffusivity

Table 2. Summary of the Diffusion Parameters in the Previous MERS Cases

Case	Age/ Sex	TTI	# of DGD	1st ADC	2nd ADC	1st FA	2nd FA	Etiology
1	14/F	5, 12 days	N/A	N/A	N/A	0.58	0.76	Dengue
2	3/F	0, 53 days	12	0.19 ± 0.03	0.82 ± 0.09	0.93 ± 0.03	0.82 ± 0.05	Mycoplasma
3	12/M	2, 9 days	12	0.49 ± 0.07	0.76 ± 0.12	0.76 ± 0.07	0.83 ± 0.10	Salmonella O9
4	28/F	3, 15 days	32	0.232	0.76	0.697	0.722	Not identified
5	8/F	1, 6 days	6	0.26	0.75	0.55	0.71	Influenza A

TTI: Time to imaging from the onset of neurological symptoms, initial and follow up.
# of DGD: The number of diffusion gradient directions
Case 1 from reference (4); Case 2-3 from reference (2); Case 4 from reference (3); Case 5 from reference (1).

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